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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,020	11/08/2000	Christoph Benning	MSU-04769	3130

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/709,020	BENNING ET AL.	
	Examiner	Art Unit	
	Yong D Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,13 and 15-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13 and 15-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 13 and 15-40 are pending.

Response to Arguments

Applicant's arguments filed on July 28, 2004 have been fully considered but they are not persuasive.

Claims 1, 13, 15-22 and 35-39 remain rejected under 35 U.S.C. 103(a) as being obvious over Benning and Essigmann et al. in view of McNally et al.

Claims 23-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Benning and Essigmann et al. in view of McNally et al. as applied to claims 1, 13, 15-22 and 35-39 above, and further in view of Bidney et al.

Claims 32-34 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Benning, Essigmann et al. and McNally et al. and Bevan et al. as applied to claims 1, 13, 15-16, 26-31 and 40 above, and further in view of Bidney et al.

Claims 1, 13, 15-16, 26-31 and 40 remain rejected under 35 U.S.C. 103(a) as being obvious over Benning, Essigmann et al. and McNally et al. in view of Bevan et al.

Applicants argue that Benning and Essigmann fail to disclose the method claimed. Applicants argue that Benning and Essigmann do not teach the expression of

both genes (SQDB and SQDX) in a host cell. This is correct. McNally et al. was used to demonstrate expression of two genes in one host cell.

Regarding the sulfite as the sulfur donor, Essigmann outlines how sulfite may act as the sulfur donor. In forming UDP-SQ, one of ordinary skill in the art would have been motivated to use sulfite as the sulfur donor upon reading the teachings of Essigmann (citedon previous PTO-892 – Archives of Biochemistry and Biophysics, 1999, page 40, 3rd paragraph). Also, one of ordinary skill in the art would have had a reasonable expectation of success of forming UDP-SQ using sulfite as the sulfur donor upon reading the teachings of Essigmann.

Applicants also argue that the phrase "as evidenced by Guler et al." is meant to indicate since Guler et al. provides no teaching of the structural information of sqdX. Guler et al. Benning teaches that "a novel sulfolipid gene in Synechococcus sp. PCC7942, designated sqdX" was identified (page 59, 1st full paragrph). Guler et al. was cited as evidence that the sqdX from Synechococcus sp. PCC7942 is 100% identical to SEQ ID NO:1. Guler et al. cites GenBank accession no. AF155063 on page 543, 2nd paragraph (GenBank accession no. AF155063 was cited on form PTO-892 – May 9, 2001) and it validates that the sqdX gene is 100% identical to SEQ ID NO:1.

Applicants argue that the McNally et al. references do not teach a method of creating an enzymatic pathway to generate a product. Applicants argue that protein co-

expression as well known in the art is mere wishful thinking. It is not mere wishful thinking. Dong et al., Kovach et al, Yue et al., Bidney et al., and Bishop et al. all teach co-expression of proteins.

Applicants argue that there is no example in the references that involves the co-expression of two enzymes in a pathway to synthesize a product. In the instant invention, the two enzymes also do not produce a product. SQDB produces UDP-SQ and SQDX produces SQDG. Dong et al., Kovach et al, Yue et al., Bidney et al., and Bishop et al. were cited to demonstrate that co-expression of two enzymes are well established in the art. One of ordinary skill in the art would have been motivated to produce using genetic engineering techniques to insert sequence encoding the desired enzymes into a plasmid to produce SQDG instead of synthesizing by chemical synthesis. The motivation of making SQDG in once process where both enzymes are present is that steps in purifying the intermediate product maybe avoided. Alternatively, the motivation of making SQDG in multiple steps is that isolation/purification of the intermediate product may increase the efficiency of the catalysis. An efficient production of SQDG is attractive because sulfolipids are possible anti-tumor and anti-HIV therapeutics. One of ordinary skill in the art would have had a reasonable expectation of success since co-expression of proteins are well known in the art.

Applicants argue that the Bevan et al., as a "naked GenEmbl report", no teachings are present to make and use these sequences to create an enzymatic pathway. It is not clear what a naked GenEmbl report is. Nevertheless, Bevan et al. teaches a sqdX gene having 100% sequence identity to SEQ ID NO:3, which can be used for enzymatic synthesis of SQDG.

Applicants argue that Dong et al., Kovach et al., and Yue et al. do not teach that co-expression of proteins is well known in the art. Dong et al., Kovach et al., and Yue et al. were cited to establish that co-expression of protein was well known at the time of filing of the instant invention, not that the references themselves teach co-expression of proteins was well known in the art. The three references all teach method of creating vector constructs to co-express proteins.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 13, 15-22 and 35-39 are rejected under 35 U.S.C. 103(a) as being obvious over Benning and Essigmann et al. in view of Toth et al.

Benning (form PTO-1449 - *Annual Review of Plant Physiology & Plant Molecular Biology*, 1998, Vol. 49 Issue 1, p53-75) teach SQDG biosynthesis using a SQDB protein and a sqdX protein (page 61, 2nd paragraph). Benning teaches the use of a SQDB protein for the production of UDP-SQ from UDP-glucose and the use of a sqdX protein for the production of SQDG from UDP-SQ (figure 3, page 62). Benning teaches that sqdX from Synechococcus sp. catalyzes the reaction of UDP-SQ into SQDG. SqdX is identical to SEQ ID NO:1 of the instant invention, as evidenced by Guler et al. (page 545, 1st paragraph – cited on previous form PTO-892).

Benning also teach that sulfite can be used as the sulfur donor (page 66, 2nd paragraph). Benning et al. also teach that SQDG of photosynthetic bacteria and plants are a promising anti-tumor and anti-HIV therapeutic (page 54, 1st paragraph).

The difference between the reference of Benning and the instant invention is that the reference of Benning does not teach a method of producing UDP-SQ from UDP-glucose with the polypeptide encoded by SEQ ID NO:6.

Essigmann et al. (cited on previous form PTO-892) teach a polypeptide, plant SQD1, that catalyzes the formation of a UDP-sulfoquinovose from UDP-glucose and is orthologous to the SQDB protein of Benning (page 31, 4th paragraph and page 39). The SQD1 gene is 100% identical to SEQ ID NO:6 of the instant invention (GenEmbl database – Accession # AF022082). Essigmann et al. teach that said SQD1 gene and the bacterial SQDB gene of Benning are the only sulfolipid genes known to be conserved between different organisms (page 31, 5th paragraph).

Although Essigmann et al. states that the sulfur donor is unknown, Essigmann et al. teaches that a sulfite is a plausible sulfur donor (page 40, 3rd paragraph).

Toth et al. (U.S. Patent No. 4,774,180 - form PTO-892) teaches a method for constructing polyprotines which can perform multiple sequential activities (abstract). Toth et al. teaches that the "primary advantage of polyproteins is that a single polyprotein with multiple activities is produced. Another advantage is that the method affords the opportunity to build polyproteins which facilitate "channeling", or the direct passage of the product of one protein, such as an enzyme to another protein, such as a

second enzyme, without passage of the intermediate compound into the solution. Channeling provides a means to sequester and act quickly on highly unstable intermediate compounds which might decay rapidly in free solution." (Column 3, lines 22-30).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute the SQDB protein of Benning with the SQD1 protein of Essigmann et al. using recombinant techniques readily available in the art. Since the SQD1 gene and the bacterial SQDB gene are the only sulfolipid genes known to be conserved between different organisms, one of ordinary skill in the art would have been motivated to interchange the two proteins, possibly to increase the efficiency of SQDG synthesis. It would have been obvious to one having ordinary skill in the art to carry out the synthesis of SQDG in one system by making a polyprotein comprising of the two enzymes, SQDB and SQDX. The motivation of making SQDG in once process where both enzymes are present is that steps in purifying the intermediate product maybe avoided. An efficient production of SQDG is attractive because sulfolipids are possible anti-tumor and anti-HIV therapeutics. One of ordinary skill in the art would have had a reasonable expectation of success since Benning outlines the pathway for SQDG production and production of a product using heterologous or orthologous enzymes are routinely performed in the art.

Claims 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benning and Essigmann et al. in view of Toth et al. as applied to claims 1, 13, 15-22 and 35-39 above, and further in view of Comai et al.

The combined references of Benning, Essigmann et al. and Toth et al. teach a method of producing sulfoquinovosyl diacylglycerol, as discussed above.

The difference between the combined teachings of Benning, Essigmann et al. and Toth et al. and the instant invention is that the cited references do not teach expression of the two proteins in plant cells.

Comai et al. (U.S. Patent No. 5,106,739 –form PTO-892) teach a method of expressing heterologous proteins in plant cells (abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to transform plant cells with the method taught by Comai et al. The motivation of applying the teachings of Comai et al. is to produce SQDG in plant host cells. One of ordinary skill in the art would have had a reasonable expectation of success since production of heterologous proteins in plant cells are performed routinely in the art.

Claims 1, 13, 15-16, 26-31 and 40 are rejected under 35 U.S.C. 103(a) as being obvious over Benning, Essigmann et al. and Toth et al. in view of Bevan et al.

Benning, Essigmann et al. and Toth et al. in combination teach a method of making SQDG biosynthesis using a SQDB protein and a sqdX protein, as discussed above.

The difference between the references and the instant invention is that the references do not teach a method of producing SQDG from UDP-SQ with the polypeptide encoded by SEQ ID NO:3.

Bevan et al. (cited on previoius form PTO-892) teach a sqdX gene which is 100% identical to SEQ ID NO: 3. The sqdX protein of Bevan et al. and the sqdX protein of Benning et al. are both from *Cyanobacterium synechococcus*.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute the sqdX protein of Benning with the sqdX enzyme of Bevan et al. Since the sqdX proteins of Benning and Bevan are homologous proteins, one of ordinary skill in the art would have been motivated to interchange the two enzyme, possibly to increase the efficiency of SQDG synthesis. It would have been obvious to one having ordinary skill in the art to carry out the synthesis of SQDG in one system. The motivation of making SQDG in once process where both enzymes are present is that steps in purifying the intermediate product maybe avoided. An efficient production of SQDG is attractive because sulfolipids are possible anti-tumor and anti-HIV therapeutics. One of ordinary skill in the art would have had a reasonable expectation of success since Benning outlines the pathway for SQDG production and

production of a product using heterologous or orthologous enzymes are routinely performed in the art.

Claims 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benning, Essigmann et al. and Toth et al. and Bevan et al. as applied to claims 1, 13, 15-16, 26-31 and 40 above, and further in view of Comai et al.

The combined references of Benning, Essigmann et al. and Toth et al. and Bevan et al. teach a method of producing SQDB, as discussed above.

The difference between the references and the instant invention is that the cited references do not teach transformation of monocotyledonous and dicotyledonous plant cells.

Comai et al. (U.S. Patent No. 5,106,739 –form PTO-892) teach a method of expressing heterologous proteins in plant cells (abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to transform plant cells with the method taught by Comai et al. The motivation of applying the teachings of Comai et al. is to produce SQDG in plant host cells. One of ordinary skill in the art would have had a reasonable expectation of success since production of heterologous proteins in plant cells are performed routinely in the art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner

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